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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,378	11/09/2001	Jeffrey T. Blue	20455P	8714
210	7590	08/23/2005	EXAMINER	
MERCK AND CO., INC			LE, EMILY M	
P O BOX 2000			ART UNIT	
RAHWAY, NJ 07065-0907			PAPER NUMBER	

1648

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/030,378

Applicant(s)

BLUE, JEFFREY T.

Examiner

Emily Le

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 18 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 18 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. The following office action is a non-final office action. This office action is non-final to allow entry of rejection(s) that has not been introduced into the record.

Status of Claims

2. Claims 1-8 and 18-19 are pending and under examination.

Claim Rejections - 35 USC § 112

3. Claims 1-8 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not readily apparent what kind or type of viral activity is encompassed by the claimed invention. Does viral activity encompass viral potency, viral stability, and/or the ability to induce caspase-3 activity? In the instant, the Office defines "viral activity" as viral stability and viral potency. This definition is in accordance with Applicant's disclosure, lines 27-30 of page 1. In the instant, the specification discloses the practice of the same method as claimed to render a conclusion on viral stability and viral potency. The Office's interpretation of "viral activity" has been communicated to Applicant in the final Office action and Advisory Action issued 11/17/2004 and 04/21/2005, respectively.

In response to the Office's position, interpretation, for "viral activity", Applicant submits that the specification does not define "viral activity" as viral stability and potency. [02/07/2005 and 05/06/2005 submissions] Applicant's submissions contradict the disclosure; hence, a 112, 2nd rejection is necessary for the recitation: viral activity.

Additionally, the specification, particularly the abstract, teaches that assaying viral induction of caspase-3 activity can be used for evaluating the stability of a virus in different formulations. However, it is not readily apparent from the claims how the measurement of caspase-3 activity can be used to evaluate the stability of the virus. The claims do not set forth a quantitative correlation between the level of caspase 3 activity and viral stability. In other terms, if the virally induced caspase 3 activity is 8000 RFU; then, at that level of caspase 3 activity, is virus considered stable? In the instant, such correlation is lacking. Ergo, the claims are rendered indefinite for it is unclear how measured caspase 3 activity correlates with viral stability.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Banki et al.¹

The claims are directed for assaying activity of a virus via the measurement of caspase 3 activity comprising the following active method steps:

a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and

¹ Banki et al. Molecular ordering in HIV-induced apoptosis. The Journal of Biological Chemistry. May 08, 1998; Vol. 273, No. 19, 11944-11953.

b) measuring said caspase 3 activity, wherein the measured caspase 3 activity serves as an indication of viral activity.

The claims also require that the caspase 3 activity be measured using a caspase 3 substrate linked to a fluorimetric or colorimetric moiety, wherein the substrate is Asp-Glu-Val-Asp (DEVD). Additionally, the claims require that the claimed method be repeated at two or more different time intervals via the practice of the active method steps at two or more time intervals.

Banki et al. teaches a method of measuring caspase 3 activity comprising the following active steps: a) contacting cells that are susceptible to caspase 3 induction with a virus, wherein the virus induces caspase 3 activity, and b) measuring said caspase 3 activity. [See particularly Figure 2 with caption, page 11946; 1st sentence, last full paragraph, page 11948; and Figure 5 with caption, page 11949]

Banki et al. also teaches the use of a caspase 3 substrate linked to a fluorimetric or colorimetric moiety to measure caspase 3 activity. The substrate that Banki et al. teaches is Asp-Glu-Val-Asp (DEVD).

Additionally, Banki et al. also repeated the method at two or more different time intervals via the practice of the active method steps at two or more time intervals.

In the instant, Banki et al. teaches the claimed invention. Banki et al. teaches the same method as claimed, while using the same active method steps that are recited in the claims. Ergo, Banki et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 4-5 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Duncan et al.²

The claims require that the virus be measles, mumps or rubella virus; and that the cells be Vero or RK-13 cells.

Duncan et al. teaches that that rubella virus induces apoptosis in Vero and RK13 cells. To quantify rubella virus induced apoptosis, Duncan et al. quantified the number of detached cells as an indicator of apoptosis.

Duncan et al. does not teach the measurement of caspase 3 activity as an alternative procedure to quantify virally induced apoptosis, as provided by Banki et al.

Banki et al. teaches the measurement of caspase 3 activity to quantify viral induced apoptosis, as noted above for claims 1-3.

Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to quantify viral induced apoptosis by measuring caspase 3 activity. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to facilitate an alternative method of quantifying virally induced apoptosis. One of ordinary skill in the art at the time the invention was

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made would have had a reasonable expectation of success for doing so because the measurement of caspase 3 activity is an art recognized method for measuring virally induced apoptosis. Thus, absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing the claimed invention.

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Wu et al.³

Claim 6 requires that prior to contacting the virus with the cell that the virus be lyophilized.

The relevance of Banki et al. as it pertains to claims 1-3 is discussed above. In the instant, it is not readily apparent if Banki et al. lyophilizes the virus. However, it is noted that Banki et al. does teach storing aliquots of supernatants with viral titers by freezing the aliquots at -70 degrees C.

Wu et al. teaches that lyophilization improves the stability of viral vaccine and recombinant protein products.

Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to lyophilize the virus. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to improve the stability of the viral supernatant. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because

² Duncan et al. Rubella virus-induced apoptosis varies among cell lines and is modulated by Bcl-XI and caspase inhibitors. Virology, March 01, 1999, Vol. 255, 117-128.

³ Wu et al. U.S. Provisional No. 60/108606 [lines 5-10, page 3], as evidenced by U.S. Patent No. 6,689,600.

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the art recognizes that lyophilization improves the stability of viral vaccine and recombinant protein products. Thus, absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing the claimed invention.

9. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banki et al., as applied to claims 1-3, in view of Goodrich, Jr. et al.⁴

Claim 8 requires that the cells be frozen then thawed.

The relevance of Banki et al. as it pertains to claims 1-3 is discussed above. In the instant, Banki et al. does not teach the freezing and thawing of the cells prior to contacting the cells with the virus.

However, Goodrich et al. does teach a method of storing cells by freezing the cells and later thawing the cells for use.

Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to freeze and thaw the cell. One of ordinary skill in the art at the time the invention was made would have been motivated to freeze the cells to allow storage of the cells, and thaw the frozen cells to use the cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the freezing and thawing of cells is well recognized in the art as a method of storing cells. Thus, absent evidence to the contrary, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing the claimed invention.

⁴ Goodrich, Jr. et al. U.S. Patent No. 5958670.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903.

The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


E. Le


Jeffrey S. Parkin, Ph.D.
Primary Patent Examiner
Art Unit 1648